

What is Claimed:

- 5           1.       A method for identifying an agent capable of enhancing longevity,  
              comprising:  
                  contacting an organism having a deregulated neurotransmitter signaling pathway  
                  with a test agent, wherein a detectable phenotype is associated with said deregulated  
                  neurotransmitter signaling pathway;  
10            assaying for the ability of the test agent to effect said phenotype,  
                  wherein the agent is identified based on its ability to alter said phenotype as  
                  compared to a suitable control.
2.       The method of claim 1, wherein said organism further has a deregulated  
15           insulin signaling pathway, wherein said detectable phenotype is associated with said  
              deregulated neurotransmitter signaling pathway or said deregulated insulin signaling  
              pathway.
3.       The method of claim 1 or 2, wherein said neurotransmitter signaling  
20           pathway is a cholinergic pathway.
4.       The method of claim 3, wherein said organism has a deregulated  
              neurotransmitter signaling pathway molecule selected from the group consisting of a  
              muscarinic receptor, EGL-30 and EGL-8, or a mammalian orthologue of said signaling  
25           pathway molecule
5.       The method of claim 1 or 2, wherein said neurotransmitter signaling  
              pathway is a serotonergic pathway.
- 30           6.       The method of claim 5, wherein said organism has a deregulated  
              neurotransmitter signaling pathway molecule selected from the group consisting of a

serotonin receptor, CAT-1, GOA-1 and DGK-1, or a mammalian orthologue of said signaling pathway molecule.

7. The method of claim 1 or 2, wherein said organism has a deregulated neurotransmitter signaling pathway molecule which is downstream of diacylglycerol (DAG) in a cholinergic or serotonergic pathway.

8. The method of claim 7, wherein said organism has a deregulated neurotransmitter signaling pathway molecule selected from the group consisting of UNC-13, PKC, UNC-18, UNC-64, SNAP-25, synaptobrevin, UNC-31, or a mammalian orthologue of said signaling pathway molecule.

9. The method of claim 2, wherein said organism has a deregulated insulin signaling pathway molecule selected from the group consisting of DAF-2, AAP-1, IRS, AGE-1, PDK-1, AKT-1, AKT-2 and DAF-18, or a mammalian orthologue of said signaling pathway molecule.

10. The method of claim 1 or 2, wherein said phenotype is increased lifespan.

11. The method of claim 1 or 2, wherein said phenotype is decreased lifespan.

12. The method of claim 1 or 2, wherein said phenotype is constitutive dauer formation.

13. The method of claim 1 or 2, wherein said phenotype is defective dauer formation.

14. A method for identifying an agent capable of enhancing longevity, comprising:

contacting an organism with a test agent, said organism having a neurotransmitter signaling pathway;

assaying for the ability of the test agent to affect an indicator of said neurotransmitter signaling pathway,

wherein the agent is identified based on its ability to alter said indicator as compared to a suitable control.

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15. A method for identifying an agent capable of enhancing longevity, comprising:

contacting an organism with a test agent, said organism having a neurotransmitter signaling pathway and an insulin signaling pathway;

10 assaying for the ability of the test agent to affect at least one indicator of neurotransmitter signaling or insulin signaling,

wherein the agent is identified based on its ability to alter said indicator as compared to a suitable control.

15 16. The method of claim 14 or 15, wherein the indicator is a signaling pathway molecule or a reporter of said molecule.

17. The method of claim 16, wherein the agent is identified based on its ability to alter expression of said indicator

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18. The method of claim 16, wherein the agent is identified based on its ability to alter an intracellular or extracellular level of said indicator

19. The method of claim 16, wherein the agent is identified based on its  
25 ability to alter an activity of said indicator

20. The method of claim 16, wherein the agent is identified based on its ability to alter the cellular localization of said indicator.

30 21. The method of any one of claims 1, 2, 14 and 15, wherein the organism is a nematode.

22. The method of claim 21, wherein the nematode is *C. elegans*.

23. The method of claim 21, wherein the nematode is a parasitic nematode.

5        24. A method for identifying an agent capable of enhancing longevity,  
comprising:

contacting a cell with a test agent, said cell having a neurotransmitter signaling  
pathway;

detecting an indicator of said neurotransmitter signaling pathway;

10        wherein an agent is identified based on its ability to modulate the  
neurotransmitter signaling pathway in said cell.

25. A method for identifying an agent capable of enhancing longevity,  
comprising:

15        contacting a cell with a test agent, said cell having a neurotransmitter signaling  
pathway and an insulin signaling pathway;

detecting an indicator of said neurotransmitter signaling pathway or insulin  
signaling pathway;

20        wherein an agent is identified based on its ability to modulate the  
neurotransmitter signaling pathway or insulin signaling pathway in said cell.

26. A method for identifying an agent capable of enhancing longevity,  
comprising:

25        contacting a cell population with a test agent, said population comprising a cell  
having a neurotransmitter signaling pathway and a cell having an insulin signaling  
pathway;

detecting an indicator of the neurotransmitter signaling pathway or insulin  
signaling pathway;

30        wherein an agent is identified based on its ability to modulate the  
neurotransmitter signaling pathway or insulin signaling pathway.

27. The method of any one of claims 24-26, wherein the neurotransmitter signaling pathway is a serotonergic pathway.

28. The method of any one of claims 24-26, wherein the neurotransmitter  
5 signaling pathway is a cholinergic pathway.

29. The method of any one of claims 24-26, wherein the neurotransmitter signaling pathway is a gamma-aminobutyric acid (GABA) signaling pathway.

10 30. The method of any one of claims 24-26, wherein the agent is identified based on its ability to activate neurotransmitter signaling in said cell.

31. The method of any one of claims 24-26, wherein the agent is identified based on its ability to inhibit neurotransmitter signaling in said cell.  
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32. The method of any one of claims 25-26, wherein the agent is identified based on its ability to modulate neurotransmitter signaling and insulin signaling.

33. The method of any one of claims 24-26, wherein the indicator is a  
20 signaling pathway molecule or a reporter of said molecule.

34. The method of claim 33, wherein the agent is identified based on its ability to alter expression of said indicator

25 35. The method of claim 33, wherein the agent is identified based on its ability to alter an intracellular or extracellular level of said indicator

36. The method of claim 33, wherein the agent is identified based on its ability to alter an activity of said indicator  
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37. The method of claim 33, wherein the agent is identified based on its ability to alter the cellular localization of said indicator.

38. The method of any one of claims 24-26, wherein the cells are mammalian cells.

5 39. The method of any one of claims 24-26, wherein the cells are human cells.

40. The method of any one of claims 24-26, wherein the cells are derived from a nematode.

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41. The method of claim 26, wherein the cell population comprises presynaptic cells and postsynaptic cells.

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42. The method of claim 41, wherein the presynaptic cells are nerve cells.

43. The method of claim 41, wherein the postsynaptic cells are nerve cells.

44. The method of claim 41, wherein the postsynaptic cells are muscle cells.

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45. A method for identifying an agent capable of enhancing longevity, comprising:

contacting an assay composition with a test compound, wherein said assay composition comprises a neurotransmitter signaling pathway molecule;

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detecting activity or expression of said neurotransmitter signaling pathway molecule;

wherein said agent is identified based on its ability to modulate activity or expression of said neurotransmitter signaling pathway molecule.

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46. The method of claim 45, wherein said agent is identified based on its ability to inhibit activity or expression of said neurotransmitter signaling pathway molecule.

47. The method of claim 45, wherein said agent is identified based on its ability to enhance activity or expression of said neurotransmitter signaling pathway molecule.

5 48. The method of claim 45, wherein said assay composition is a cell-free extract.

49. A novel agent identified according to the method of any one of claims 1, 2, 14, 15, 24, 25, 26 and 45.

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50. A pharmaceutical composition comprising the agent of claim 49.

51. A method of enhancing longevity in a subject, comprising:  
administering to a subject in need of enhanced longevity a pharmacologically  
15 effective dose of an agent that modulates a neurotransmitter signaling pathway molecule;

wherein modulation of said neurotransmitter signaling pathway molecule in said subject enhances longevity.

20 52. The method of claim 51, wherein the agent modulates expression or activity of said neurotransmitter signaling pathway molecule.

53. The method of claim 51, further comprising administering a pharmacologically effective dose of an agent that inhibits an insulin signaling pathway  
25 molecule.

54. The method of any one of claims 51-53, wherein said subject is an aging or aged subject.

30 55. The method of any one of claims 51-53, wherein said subject exhibits at least one symptom of premature aging.

56. The method of any one of claims 51-53, wherein said subject has an aging-associated disorder.